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SO VETERINARY PARASITOLOGY, (MAY 1993) Vol. 47, No. 3-4, pp. 225-233.

SO Z PARASITENKD, (1983) 69 (1), 27-34.*

SO Revista Brasileira de Parasitologia Veterinaria, (1995) Vol. 4, No. 1, pp.* 15-19.

SO Vet.Rec. (111, No. 18, 414-15, 1982) 2 Fig. 2 Tab. 12 Ref.*

SO J PROTOZOOL, (1987) 34 (4), 398-402.

SO AM J TROP MED HYG, (1987) 36 (3), 505-508*

Applied and Environmental Microbiology, (1995) Vol. 61, No. 2, pp.*

SO Journal of Parasitology, (Feb., 1998) Vol. 84, No. 1, pp. 8-15.

SO Journal of the Egyptian Society of Parasitology, (Aug., 1999) Vol. 29, No. 2, pp. 551-560. *

SO FEMS Microbiology Letters, (1994) Vol. 118, No. 1-2, pp. 45-49.

SO J.Protozool. (35, No. 4, 583-89, 1988) 7 Fig. 2 Tab. 20 Ref. *

SO AM J TROP MED HYG, (1987) 36 (3), 505-508. *

SO J PARASITOL, (1976) 62 (2), 199-202.

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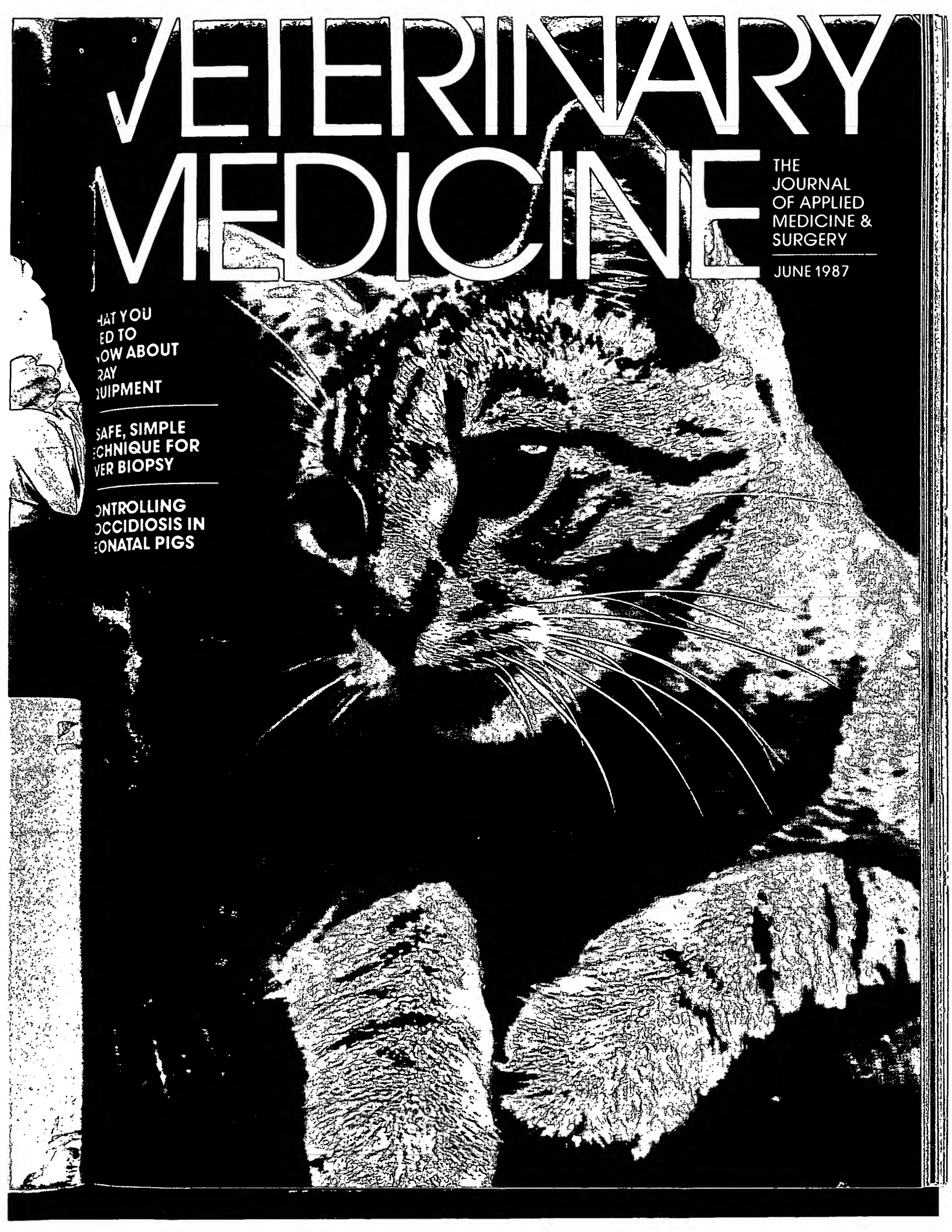

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ONTROLLING
OCCIDIOSIS IN
ONATAL PIGS

Controlling coccidiosis in neonatal pigs

Isospora suis is responsible for significant losses among piglets because damage to the intestinal mucosa frequently precedes diagnosis. Here are the techniques you'll need to prevent the problems associated with this pathogen.

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DURING THE PAST DECADE, neonatal diarrhea due to the coccidium *Isospora suis* has become a significant problem in the U.S. swine industry. Epidemiologic studies have revealed the organism's presence in all types of management systems and farrowing facilities.[1-5] From July 1, 1982, until June 30, 1983, *I. suis* was the most commonly isolated enteric pathogen from nursing pigs necropsied at the Illinois State Diagnostic Laboratory.[6]

Treating clinically affected pigs is unrewarding because the sexual stages of the organism are refractory to treatment, and by the time a diagnosis is made, the intestinal mucosa is irreversibly damaged.[7] Controlling the organism, therefore, is the only recourse to prevent significant losses.

Diagnosing infection

Because *I. suis* does not respond to antibiotics or other treatments for neonatal diarrhea, a correct diagnosis is essential in order to institute preventive measures. In addition to the history, clinical signs, gross pathology, and histopathology, a diagnosis is based on stained impression smears or smears made from mucosal scrapings.[8,9] Fecal examinations may be helpful occasionally, but they are not consistently reliable diagnostic tools for clinical coccidiosis in pigs.

The typically described history is diarrhea that is unresponsive to antibiotic treatment, primarily in five- to 14-day-old piglets.[1,2,6,10] Six- to 10-day-old pigs are most commonly affected.[6,11] Healthier pigs within a litter are often affected first.[3] In the early stages of infection, pigs become less active, choosing to lie near a heat source.[6] Morbidity is variable but may reach 100 percent. Mortality is usually low but may increase tremendously when other enteric pathogens are present.[3,11,12]

Reportedly, infection peaks in late summer and early fall (July, August, September).[6,11] The primary clinical sign is diarrhea, which usually is pasty at first, but which rapidly becomes fluid, lasting up to five or six days if the pig survives the episode. Dehydration, weight loss, and unthriftiness are consistent clinical signs. Sporadic vomiting may occur, and stunting is often a sequela.

Fecal flotations are not reliable diagnostic tests in clinical cases of coccidiosis. Negative results are meaningless, and although positive results are significant, they are not often obtained until the disease has progressed to an advanced stage.

Fecal exams may be useful in screening for the organism's presence, or in estimating its prevalence in a herd,[5] but they cannot be relied upon in an outbreak.

If fecal exams are performed and coccidian oocysts are found, they may be identified as *I. suis* by the presence of one of the following: 1) one or more "hazy bodies" beneath the oocyst cell wall when the oocyst is in the unsporulated stage, or 2) a two-celled sporoblast when the oocyst has sporulated.

The presence of either hazy bodies, the two-celled sporoblast, or both in a fecal flotation test is diagnostic for *I. suis*. By using these criteria, a practitioner can avoid taking the time and trouble necessary for sporulation of the organism in the laboratory.[8]

Gross lesions of coccidiosis cannot be distinguished from those of other enteric pathogens found in baby pigs. A fibrinonecrotic, diphtheritic pseudomembrane in the ileum or jejunum is considered the classic lesion, but this change is found only in severe cases.[8,11,13,14] Other gross lesions may include thin-walled, hyperemic, fluid-filled small intestines; empty lacteals; milk curd in the stomach; and enlarged mesenteric lymph nodes.[15]

Histopathology is a reliable and widely used diagnostic method, but the process is time-consuming and expensive.[8,9] Histopathologic lesions include multifocal villous atrophy and blunting in the ileum and middle and lower jejunum, and the presence of endogenous stages of the organism within parasitophorous vacuoles beneath the nucleus of villous epithelial cells.[5]

Mucosal impression smears and smears of mucosal scrapings are reliable, rapid, inexpensive, and practical techniques for diagnosing coccidiosis in pigs. Stained smears from the jejunum and ileum (Diff-Quick Stain Set — Harleco) will contain both asexual and sexual stages of the organism. The most common forms are the merozoites, which are dark staining and crescent- to comma-shaped.

Smears should be made from grossly affected areas or from several different segments if gross changes are not evident. Always examine more than one pig and do not use pigs that have been dead for more than a few minutes.[8,9]

Diagnosing *I. suis* during an outbreak of diarrhea can be difficult; therefore, you may need to combine diagnostic procedures to differentiate coccidiosis from other pathogens commonly associated with the porcine neonatal diarrhea complex: Rotavirus, transmissible gastroenteritis virus, *E. coli*, *Clostridium perfringens* type C, and *Strongyloides ransomi*.

Prevention and control

Sanitation effective enough to reduce the exposure of baby pigs to infective organisms is the basis for prevention and control of diarrhea due to *I. suis*. Sanitation begins with the sow before it enters the farrowing house. The sow should be scrubbed with a mild disinfectant, and farrowing crates should be cleaned thoroughly and disinfected between groups of sows.

Both physical cleaning and the

Controlling coccidiosis: The recommended practices

Based on the current knowledge of the epidemiology of *Isospora suis*, the following practices have been suggested as control methods for porcine neonatal coccidiosis:[8,19]

1. Correct diagnosis is essential. Distinguish *I. suis* from other pathogens of the neonatal swine diarrhea complex. Antibiotics are not effective against infection with *I. suis*.
2. Limit access by workers to farrowing crates; this will slow down or perhaps prevent crate-to-crate spread of *I. suis* oocysts.
3. Wash farrowing crates thoroughly to remove fecal material and then disinfect them between groups of sows. Steam cleaning after washing is recommended. Commercial bleach or ammonia solutions (50% aqueous) appear to be the most effective disinfectants. Do not mix bleach and ammonia. Because these solutions can be irritating to skin and mucous membranes, they should be used with care.
4. If sows are the major source of *I. suis* contamination, add coccidiostats to sow rations two to three weeks before farrowing and throughout lactation.

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use of disinfectants are important, because disinfectants will not penetrate organic material and coccidial oocysts resist many common disinfectants (*Tables 1 & 2*).[16] Commercial bleach or ammonia solutions (50% aqueous) appear to be the most effective disinfectants. Steam cleaning, high-pressure water, and direct heat — followed by concentrated disinfectants allowed to remain unrinsed for several days before sows enter the unit — are measures that have been used with some degree of success.[8,16,17]

Once the sow has entered the crate, fecal material should be removed daily. Daily removal of oocysts will decrease the exposure risk to baby pigs.[18] Limiting the movement of workers among farrowing crates and houses (by assigning a single worker to a house or group of crates) will slow or prevent the spread of the organisms.

Medicating baby pigs to control coccidiosis has been attempted, but to be effective the medication must begin before clinical signs of disease are seen. This means instituting a preventive regimen at one to three days of age. Amprolium has been used most commonly for this purpose, but decoquinate and sulfaquinoxaline also have been used, with mixed results.[1,14,19-22]

Using these medications for prevention also requires either a separate water line to the baby pigs, or individual daily dosing. Producers usually cannot or will not dose baby pigs individually each day, and the amount of water that a nursing piglet drinks in the first few days of life may be insufficient to deliver an effective dose of medication.

Another possible control of coc-

TABLE 1
Results of Sporulation of *Isospora suis* Oocysts in Household Disinfectants*

	Sporulated (%)	
	After 60 Hours	After 120 Hours
Dichromate 2.5%**	86	90
Sulfuric acid 2%**	82	84
Household ammonia 100%	0	0
Household ammonia 50%	0	0
Household ammonia (8 oz/gal water)	0	5
Household ammonia (2 oz/gal water)	55	77
Lysol (4 oz/gal water)	8	12
Chlorox 100%	0	0
Chlorox 50%	15	0
Chlorox (8 oz/gal water)	63	68
Chlorox (1 oz/gal water)	86	88

*Table taken from Reference 16.
**These products served as control solutions for sporulation.

TABLE 2
Results of Sporulation of *Isospora suis* Oocysts in Commercial Disinfectants*

	Sporulated (%)	
	After 60 Hours	After 120 Hours
Dichromate 2.5%**	86	90
Sulfuric Acid 2%**	82	84
Environ 100%	3	0
Environ (0.5 oz/gal water)***	82	77
DCR 100%	54	20
DCR (1 oz/gal water)***	87	84
IOFEC-80 50%	85	63
IOFEC-80 (1 oz/5 gal water)**	86	89
Nolvasan 100%	93	90
Nolvasan 50%	81	84

*Table taken from Reference 16.
**These products served as control solutions for sporulation.
***The manufacturer's recommended dilution.

cidiosis involves feeding coccidiostats to sows, beginning three weeks before farrowing and continuing during lactation. Amprolium, decoquinate, and monensin have been used, producing different results that could be due to differences in coccidiostats, varying dosage regimens, or to different degrees of sanitation among farms.[1,3,11,12,14,22] It should be noted, however, that no coccidiostats are FDA-approved for use in sows or baby pigs. Difficulties in developing an experimental model, in determining the exact source of the organism to the baby pig, and in developing a practical delivery system to the target animal (the neonate), have interfered with research efforts in this area.

In the field, monensin at 60 to 100 g/ton of feed seems to be more effective than other coccidiostats used in this manner, although no scientific documentation supports this idea. Nor are there any published studies determining optimum dose levels and efficacies of various coccidiostats when fed in sow rations. Despite the widespread belief that sows are the source of oocysts in baby pigs, it is rare to find a sow shedding *I. suis* (<1% in published surveys), and transmission of the organism from sows to pigs has not been documented.[2,4,9,17,19]

Control has been achieved on at least one total confinement, farrow-to-finish swine farm which made combined use of washing, phenol disinfection, steam cleaning of farrowing houses, and treatment of sows with amprolium before farrowing and during lactation.[17,23] It is impossible to attribute the observed improvement to any one of these methods. It has been suggested that the improvement seen on farms where coccidiostats are used may be due to the producer's increased awareness and strict cleaning and sanitation practices.[2]

The need for diligence

Neonatal coccidiosis, now a significant problem in the U.S. swine industry, is widespread, occurring in all types of facilities and management systems and under apparently adequate sanitation programs. Correct diagnosis and differentiation from other enteric pathogens of neonatal pigs is essential. Treatment of clinically affected pigs is usually unrewarding.

Control of the organism requires thoroughness and diligence, and above-average sanitation. Further study is needed on the sow's role in transmission and on the efficacy of coccidiostats in sow rations. At this point, it appears that a clean environment and thorough sanitation and disinfection are the most important factors in preventing and controlling the disease.

REFERENCES

1. Roberts, L.; Walker, E.J.: Field Study of Coccidial and Rotaviral Diarrhoea in Unweaned Piglets. *Vet. Rec. 110*:11-13; 1982.
2. Lindsay, D.S. *et al*: Prevalence of Oocysts of *Isospora suis* and *Eimeria* spp from Sows on Farms With and Without a History of Neonatal Coccidiosis. *JAVMA 185*:419-421; 1984.
3. Sangster, L.T. *et al*: Coccidiosis Associated with Scours in Baby Pigs. *VM/SAC 73*(10):1317-1319; 1978.
4. Nilsson, O. *et al*: Epidemiology of Porcine Neonatal Steatorrhoea in Sweden: 1. Prevalence and Clinical Significance of Coccidial and Rotaviral Infections. *Nord. Vet. Med. 36*:103-110; 1984.
5. Tubbs, R.C.; Dekich, M.A.: Neonatal Coccidiosis in Nine Large Mississippi Swine Herds. *Miss. Vet. J.*:8-10; Fall 1986.
6. Biehl, L.G.; Hoefling, D.C.: Diagnosis, Treatment, and Prevention of Diarrhea in 7- to-14-day-old Pigs. *JAVMA 188*:1144-1146; 1986.
7. Hoefling, D.C.; Todd, K.S.: Coccidiosis and Toxoplasmosis. *Disease of Swine*, 5th Ed. (A.D. Leman *et al* eds.). The Iowa State University Press, Ames, 1981; pp 590-597.
8. Lindsay, D.S. *et al*: Diagnosis of Neonatal Porcine Coccidiosis Caused by *Isospora suis*. *VM/SAC 78*(1):89-95; 1983.
9. Stevenson, G.W.; Andrews, J.J.: Mucosal Impression Smears for Diagnosis of Piglet Coccidiosis. *VM/SAC 77*:111-113; 1981.
10. Stuart, B.P. *et al*: Coccidiosis in Swine: A Search for Extraintestinal Stages of *Isospora suis*. *Vet. Rec. 110*:82-83; 1982.
11. Robinson, Y; Morin, M.: Porcine Neonatal Coccidiosis in Quebec. *Canad. Vet. J. 24*:212-216; 1983.
12. Roberts, L.; Walker, E.J.: Diarrhoea in Unweaned Piglets Associated with Rotavirus and Coccidial Infections. *Vet. Rec. 107*:156-157; 1980.
13. Sanford, S.E.; Josephson, G.K.A.: Porcine Neonatal Coccidiosis. *Canad. Vet. J. 22*:282-285; 1981.
14. Stuart, B.P. *et al*: *Isospora suis* Enteritis in Piglets. *Vet. Pathol. 17*:84-93; 1980.
15. Tubbs, R.C.: A Review of Porcine Neonatal Coccidiosis. *Mod. Vet. Prac. 67*:899-903; 1986.
16. Stuart, B.P. *et al*: Coccidiosis in Swine: Effect of Disinfectants on *in vitro* Sporulation of *Isospora suis* Oocysts. *VM/SAC 76*:1185-1186; 1981.
17. Ernst, J. V. *et al*: Control of *Isospora suis*-induced Coccidiosis on a Swine Farm. *AJVR 46*:643-645; 1985.
18. Joyner, L.P. *et al*: Coccidiosis and Coprophagy in Pigs (Correspondence) *Vet. Rec. 108*:264-265; 1981.
19. Current, W.L.: Neonatal Swine Coccidiosis: An Update. *Proc. Amer. Assn. Swine Prac.*, 1986; pp 241-252.
20. Clark, L.K.: Coccidiosis in Baby Pigs. *Mod. Vet. Prac. 61*:605-606; 1980.
21. Strutt, E.: Coccidiosis: An Elusive Cause of Baby-pig Scours. *Pork '86*:18-21; Jan. 1986.
22. Coussement, W. *et al*: Baby Pig Diarrhea Caused by Coccidiosis. *Vet. Quart. 3*:57-60; 1981.
23. Lindsay, D.S. *et al*: Control of *Isospora suis* Infection in Swine. *Mod. Vet. Prac. 64*:831; 1983.